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The role of sex, age, and BMI in treatment decisions for knee osteoarthritis: conservative management versus total knee replacement

Fabiola Ojeda[1,2], Laura Tío[2*], Francisco Castro-Domínguez[3], Simone Tassani[4], Jerome Noailly[4] and Jordi Monfort[1,2]

Abstract

Background Knee osteoarthritis (KOA) has a complex, multifactorial nature with well-established risk factors which may influence treatment decisions. Here we want to identify distinctive characteristics between patients receiving conservative treatment versus total knee replacement (TKR), analyzing both patient-specific and knee-specific features.

Methods This case–control study compared patients assigned to TKR versus conservative management, examining subjects aged 60–75 years with radiographically confirmed KOA (Kellgren–Lawrence grades 2–3), with all participants evaluated by blinded clinicians using validated assessment tools including Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), Hospital Anxiety and Depression Scale (HADs), Pain Catastrophizing Scale (PCS) and Daily physical activity (DPA) questionnaires. The study employed multivariate analysis of variance for continuous variables at both patient and knee levels, followed by univariate analysis of variance for significant factors, while logistic and linear regression analyses were used to calculate odds ratios, with Bonferroni corrections applied to adjust p-values for multiple comparisons.

Results Between 2016 and 2020, the study included 87 patients (51 women and 36 men) with a mean age of 67.7 years in both treatment groups, with a slightly higher body mass index (BMI) of 31.9 kg/m^2 in the TKR group vs 30.5 kg/m^2 in the conservative management group. TKR patients demonstrated significantly worse scores in WOMAC, HADS, and PCS compared to the conservative management group, though DPA levels remained similar between both groups. At the knee level, women demonstrated significantly higher pain sensitivity and central sensitization compared to men, with no differences between conservative and TKR groups.

Conclusions Patients undergoing TKR exhibited significantly worse baseline clinical outcomes, particularly in WOMAC scores, despite having similar radiographic severity to those receiving conservative treatment, suggesting that functional and symptomatic measures may be more valuable than radiographic findings in determining surgical intervention.

Keywords Osteoarthritis, Total knee replacement, Risk factors

*Correspondence:
Laura Tío
ltio@researchmar.net
Full list of author information is available at the end of the article

Introduction

Osteoarthritis (OA) is a degenerative joint disease characterized by the breakdown of cartilage and changes in the underlying bone and inflammation of the synovial lining, leading to pain, functional limitations, and stiffness [1]. OA is a global leading cause of disability, particularly among older adults, as it significantly impairs daily activities and overall quality of life. The disease is highly prevalent, especially in individuals over 55 years old, and is associated with a high socioeconomic burden [2, 3]. In 2019, OA ranked among the top conditions contributing to years lived with disability [4], with its impact nearly doubling since 2000 and it's reasonable to expect that the situation has potentially worsened given recent trends. The economic implications are substantial, with healthcare and non-healthcare costs related to OA estimated to account for 0.25–0.50% of gross domestic product in various countries [2, 5]. Furthermore, OA often necessitates surgical interventions, such as total joint replacement, particularly for the knee (KOA), representing approximately 70% of patients suffering from OA.

Several reviews and meta-analysis have identified various risk factors associated with the onset of KOA or knee pain [6–11]. Obesity is a well-established risk factor for KOA progression, with significant weight loss shown to reduce knee pain and improve quality of life over extended periods [12]. Other consistent risk factors across studies include previous knee trauma, older age, and female sex. However, there are also discrepancies in the findings related to potential risk factors, such as hand OA, smoking, occupational activities, and physical activity or exercise. The presence of these diverse and mixed factors underscores the heterogeneous and multifactorial nature of KOA [13], which often coexists with other medical conditions. This complexity can lead to a discordance between symptoms and structural signs, and different patients may experience varying rates of disease progression, highlighting the need to identify distinctive clinical characteristics that differentiate patients requiring conservative management versus surgical intervention, particularly when traditional radiographic findings may not fully capture the patient's clinical condition. In this context, standardized clinical assessment tools like the WOMAC have emerged as valuable instruments to quantify patients' symptoms and functional limitations. The WOMAC score has demonstrated high sensitivity and specificity for indicating total knee replacement (TKR), providing clinicians with objective measures to support surgical decision-making when radiographic findings alone may be insufficient [14].

This study aims to address this gap by evaluating clinical measures as predictors of treatment pathways, focusing on key variables such as sex, body mass index (BMI), and clinical assessment scores. This heterogeneity poses a challenge in tailoring treatments and preventive strategies, as it necessitates identifying patients with specific KOA of similar etiologies or modifiable factors. Nowadays, conservative management includes core treatment recommendations such as advice and information, local muscle strengthening and aerobic exercise, weight loss if overweight, pain relief medications, lifestyle recommendations, and intra-articular infiltrations. In contrast, surgical intervention involves TKR.

Currently research in KOA is increasingly focused on patient stratification strategies, recognizing the heterogeneous nature of the disease and the need for personalized treatment approaches. These strategies aim to categorize patients based on specific phenotypes and risk factors, moving away from the traditional "one size fits all" approach to management [15]. A recent systematic review has identified six clinical phenotypes that classify patients based on disease progression: chronic pain with a prominent central mechanism, inflammation, metabolic syndrome, bone and cartilage metabolism, mechanical overload, and minimal joint disease [16]. By stratifying patients according to these phenotypes, clinicians can better identify those at higher risk of disease progression and implement more targeted therapeutic interventions. Furthermore, the underlying mechanisms of KOA may be driven by a single factor or a combination of factors, highlighting the complexity of the disease.

This study aimed to identify distinctive clinical characteristics between patients receiving conservative management versus total knee replacement (TKR), analyzing both patient-specific and knee-specific features, while examining how traditional risk factors (sex, age, BMI) influence treatment pathways. We hypothesized that clinical assessment scores, particularly WOMAC and PCS, would be more strongly associated with TKR indication than radiographic findings or traditional risk factors.

Methods

Recruitment took place between 2016 and 2020 by an experienced osteoarthritis rheumatologist at Hospital del Mar, Barcelona, Spain. Eligible participants were individuals with radiographically established knee osteoarthritis who presented Kellgren and Lawrence (KL) scale [17] grades 2 or 3 within the past 12 months. They were at least 60 years old.

Patients who met the eligibility criteria [18], detailed in Supplementary Table 1, were invited to participate in the study. Those who agreed to participate provided written informed consent.

Study design and clinical assessment

This case–control study was designed to identify the clinical traits associated with the need for TKR in patients with KOA. The study compared patients assigned to undergo a TKR intervention to those assigned to conservative management. To ensure unbiased assessment, the clinician conducting the evaluations was blinded to the treatment group assignments, with a single-blind design maintained through separate personnel for recruitment and analysis, and patients were instructed not to disclose their group allocation to the evaluating physician.

Patient recruitment for the conservative management group (CMG) was conducted during consecutive follow-up clinical visits. All participants in this group had undergone knee radiography within the past 12 months. Participants were allocated using stratified random sampling based on age, sex, and BMI, although complete matching was not achieved for males in the TKR group despite extended recruitment efforts. The matching variables selected for this study were sex (male/female), BMI, age and DPA variables (household and the leisure domains) to ensure comparability between the TKR and CMG groups.

Primary outcome measures

The primary outcome measures included demographic and anthropometric characteristics of the participants that differentiate patients referred to CMG from those who underwent TKR: age (categorized as 60–67 years and 68–75 years), BMI, (categorized as non-obese < 30 kg/m^2 and obese ≥ 30 kg/m^2), and sex.

Secondary outcome measures

The study employed a comprehensive set of assessment tools and questionnaires measured on the same day to evaluate various aspects of patients' conditions. Pain and function of the affected joint were measured by the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) questionnaire [19]. Briefly, WOMAC is a self-administered scale ranging from 0 to 96 points, where higher scores indicate worse pain, stiffness, and functional limitations. Anxiety and depression levels were assessed with the Hospital Anxiety and Depression Scale (HADs) [20], while catastrophic thinking related to pain was evaluated using the Pain Catastrophizing Scale (PCS) [21]. Daily physical activity (DPA) in the household domain was measured using the modified-Baecke questionnaire for elderly subjects [22]. Additionally, three variables related to knee pain were evaluated using the same pressure algometer: the number of knee tender points (KTP), tenderness at the tibial site (TTS), and temporal summation. Briefly, KTP considered if the patient-reported pressure pain threshold (PPT) of less than 4 kg/cm^2 tested in the extended version of the Arendt-Nielsen peripatellar map; TTS considered the painful intensity on an 11-points numerical rating scale to a pressure of 4 kg/cm^2 applied for two seconds; and temporal summation was calculated from the difference between pain reported on an 11-point pain scale before and after ten repeated pressure stimulation on the tenderest point around the knee. Clinical pain sensitization was defined as the presence of at least two tender sites around the joint, excluding three typical painful sites in knee osteoarthritis (lateral interline, medial interline and patella) [23]. For patients with bilateral knee osteoarthritis meeting the criteria, both knees were evaluated.

Statistical analysis

Age, BMI and sex were treated as independent dichotomous variables rather than adjusting covariables in the analysis. Age was categorized in two groups (60–67 years and 68–75 years), while BMI was divided into non-obese (< 30 kg/m^2) and obese (≥ 30 kg/m^2). This approach was chosen due to the uncertainty regarding the linearity of age and BMI effects on the outcomes of interest.

For the statistical analysis, multivariate analysis of variance (MANOVA) and linear regression were employed for continuous variables, while logistic regression was used for categorical variables. The study utilized stratified random sampling for recruitment, ensuring a balanced representation of age, BMI and sex. Initially, the necessary assumptions for MANOVA were statistically tested, and variables that did not meet these assumptions were excluded from the analysis. Subsequently, MANOVA tests were conducted for clinical variables at both the patient and knee levels. For patients with bilateral KOA, each knee was analyzed as an independent observation in the statistical analysis, with knee-level variables treated as separate data points following a standard statistical approach. When a factor was found to be statistically significant in the MANOVA, a follow-up univariate analysis of variance (ANOVA) was performed. To normalize right-skewed data, logarithmic transformation was applied, while exponential transformation was employed to stabilize variance and normalize distributions. Variables that continued to exhibit non-homogeneous variance after transformation were excluded from further analysis to maintain statistical validity and ensure reliable result interpretation. Bonferroni corrections were applied to adjust p values: 0.0125 for the patient level test (four variables analyzed: WOMAC, HAD, PCS, DPA household), 0.025 for the knee level tests (two variables analyzed: KTP, TTS), and 0.0026 for the calculation of the association odds ratios (OR) (19 variables analyzed).

To estimate the OR and 95% confidence intervals (95% CI) for TKR, linear and logistic regression analyses were performed. These models were adjusted for sex, age, and BMI.

A post-hoc power analysis was performed based on the observed difference in WOMAC scores between groups. With our achieved sample size, the study had 98% power to detect a clinically meaningful difference of 16.5 points in WOMAC scores between groups at a significance level of 0.05 and in PCS scores between groups, the study had 92% power to detect a clinically meaningful difference of 7,5 points in PCS scores between groups at a significance level of 0.05.

The MANOVA tests were conducted using SPSS v.23.0 (IBM Corp., Armonk, NY, USA), while the regression analyses were performed using R version 3.5.2 (R Foundation for Statistical Computing, Vienna, Austria).

Ethics statement

The study was conducted in accordance with the principles expressed in the Declaration of Helsinki, and the protocol followed the Good Clinical Practice guidelines and was approved by the Ethical Committee of Clinical Research of the Parc de Salut Mar of Barcelona (2016/6747/I). All participants provided written informed consent.

Results

Clinical characteristics

Of the 90 selected patients, 3 were excluded due to a history of meniscectomy. Ultimately, 87 patients were included in the study of whom 51 were women (25 in the CMG group and 26 in the TKR group) and 36 were men (23 in the CMG group and 13 in the TKR group). The recruitment of participants faced some challenges, particularly in the male TKR group. Many potential male candidates had to be excluded due to previous partial or total meniscectomy procedures. Despite screening a large number of patients, we were unable to complete all planned study subgroups. Specifically, three subgroups in the male TKR category remained incomplete due to a lack of eligible participants who met the study's inclusion criteria. The average age of participants was similar in both groups, with the CMG group having a mean age of 67.7 years (Standard Deviation (SD) 4.9) and the TKR group also averaging 67.7 years (SD 4.0). Regarding the BMI, the CMG group had a mean of 30.5 kg/m^2 (SD 4.4), while the TKR group had a slightly higher average BMI of 31.9 kg/m^2 (SD 6.2).

Clinical traits at the patient level

In preparation for the multivariate analysis at the patient level, we encountered non-normal distributions in the PCS and the two DPA variables. Characteristics of the clinical traits at the patient level are described in Table 1. Briefly, patients who underwent TKR exhibited poorer outcomes in several key measures. They scored worse on average in the WOMAC (71.33 vs. 54.8), HADS (12.72 vs. 10.85), and PCS (19.64 vs. 12.17) scores, for TKR and CMG groups respectively. However, their DPA scores showed no significant differences compared to the CMG group, neither in the household or in the leisure domains (Table 1).

To address this, we applied logarithmic transformation to the PCS data and exponential transformation to the DPA variables, ensuring they met the necessary statistical assumptions for our analysis. The multivariate analysis proceeded after confirming that most assumptions were met. However, the DPA variables related to leisure exhibited non-homogeneous variance, violating one of the assumptions. Consequently, these variables were excluded from the analysis. There were no outliers across all analyses conducted.

Table 1 Demographic and anthropometric characteristics of participants

		N	Age	BMI	WOMAC	HADS	PCS	DPA	
								Household	Leisure
Treatment	CNV	48	67.71 (4.87)	30.45 (4.43)	54.77 (19.27)	10.85 (7.58)	12.17 (9.81)	17.56 (5.71)	6.94 (4.36)
	TKR	39	67.69 (3.95)	31.93 (6.18)	71.33 (15.42)	12.72 (8.66)	19.64 (9.72)	17.64 (3.20)	6.14 (5.23)
Sex	Men	36	68.56 (4.31)	31.13 (5.72)	53.06 (17.31)	9.06 (6.85)	12.75 (10.54)	16.22 (5.89)	6.37 (3.77)
	Women	51	67.10 (4.50)	31.10 (5.04)	68.65 (18.32)	13.55 (8.43)	17.47 (9.96)	18.57 (3.44)	6.73 (5.38)
Age	60–67 y	40	63.53 (2.22)	31.35 (6.07)	61.08 (19.45)	11.05 (7.98)	14.50 (10.75)	17.78 (5.07)	6.46 (5.44)
	68–75 y	47	71.26 (2.21)	30.92 (4.61)	63.15 (19.54)	12.23 (8.22)	16.38 (10.14)	17.45 (4.47)	6.67 (4.15)
BMI	≤ 30 kg/m^2	41	67.73 (4.55)	26.95 (2.43)	59.17 (18.68)	9.41 (6.61)	13.78 (10.21)	17.37 (5.09)	6.43 (4.61)
	> 30 kg/m^2	46	67.67 (4.42)	34.83 (4.31)	64.89 (19.85)	13.72 (8.79)	17.07 (10.44)	17.80 (4.43)	6.71 (4.94)

Data are presented as mean (SD) otherwise specified. BMI, body mass index; CNV, conservative; DPA, daily physical activity; HADS, hospital anxiety and depression scale; PCS, pain catastrophizing scale; TKR, total knee replacement; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index; y, years

The multivariate analysis showed significant differences between groups for the treatment and sex variables (p values: 0.004 and 0.001, respectively, Fig. 1). In particular, patients from the TKR group present significant higher values at WOMAC (CMG: 54.77, CI 95% 50.41- 59.12 vs TKR: 68.13 CI 95% 62.08–74.19; p value: 0.0006) and PCS (CMG: 9.00, CI 95% 7.44–10.88 vs TKR: 15.61, CI 95% 11.98–20.33; v-value: 0.0012) compared to the CMG group (Fig. 1). In the case of sex, variables showing significant differences were WOMAC (men: 54.16, CI 95% 48.00–60.31 vs women: 68.75, CI 95% 64.52–72.97; p value: 0.0002) and HADs (men: 8.53, CI 95% 5.393–11.66 vs women: 13.54, CI 95% 11.39- 15.694; p value: 0.0105) with PCS near significance value (men: 9.83, CI 95% 7.52–12.85 vs women: 14.28, CI 95% 11.88–17.18; p value: 0.0249; Fig. 1).

Only the differences that includes sex, age and BMI was significant in the treatment group (p value 0.006, Fig. 1). The univariate analysis showed that this was due to WOMAC and PCS values (p-value: 0.002 in both cases). Women had significantly higher total WOMAC values than men in those groups with one risk factor (age or BMI). Furthermore, WOMAC and PCS values were significantly lower in women without risk factors (younger and not obese) than in women with one risk factor (Supplementary Table 2, and Supplementary Fig. 1).

Clinical traits at the knee level

Some patients had OA in both knees, and in these cases, both joints were evaluated at the knee level. Among the joint pain assessment variables, temporal summation exhibited non-homogeneous variance and was consequently excluded from further analysis. The remaining two pain variables (KTP and TTS) met all necessary assumptions for conducting a MANOVA analysis. Regarding the severity of the KOA, as evaluated by the KL scale, no significant differences were observed between treatment groups (Table 2) and the individual joint compartments (data not shown).

Sex and age showed significant differences in the multivariate analysis (< 0.001 and 0.012, respectively, Fig. 2). Women showed significant higher values for both variables studied: KTP (men: 2,18, CI 95% 0,94–3,43 vs women: 6,84, CI 95% 5,99–7,69; p value: < 0.001) and TTS (men: 3,08, CI 95% 1,66–4,50 vs women: 6,77, CI 95% 5,80–7,74; p value: < 0.001).

Regarding central sensitization, the logistic regression analysis showed that women had a significantly higher risk of presenting central sensitization than men (OR

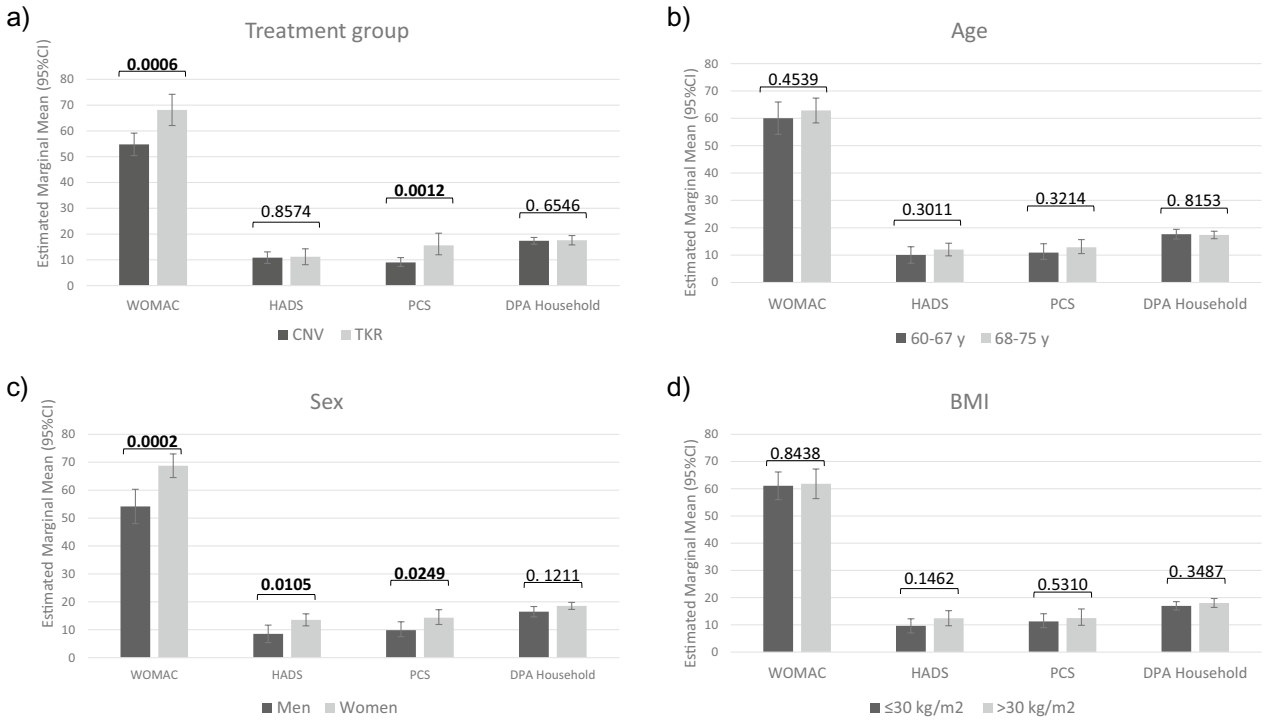

Fig. 1 Results of multivariate and univariate analysis of variables at the patient level. Significant results are shown in bold. Results are stratified by **a** treatment group between CNV and TKR, **b** age between 60–67 and 68–75, **c** sex between males and females, and **d** BMI between < 30 and ≥ 30. CNV, conservative; TKR, total knee replacement; BMI, body mass index; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index; HADs, Hospital Anxiety and Depression Scale; PCS, Pain Catastrophizing Scale

Table 2 Clinical traits at the knee level

		N (joints)	KL grade		Knee tender points	Tenderness at the tibial site	Temporal summation	Central sensitization	
			2	3				No	Yes
Treatment	CNV	59	13 (22.0%)	46 (78.0%)	4.7 (3.5)	5.0 (4.1)	1.8 (2.4)	22 (37.3%)	37 (62.7%)
	TKR	39	7 (17.9%)	32 (82.1%)	5.4 (4.0)	6.2 (3.5)	1.9 (2.1)	14 (37.8%)	23 (62.2%)
Sex	Men	40	6 (15.0%)	34 (85.0%)	2.4 (2.7)	3.8 (3.5)	1.4 (1.9)	27 (67.5%)	13 (32.5%)
	Women	58	14 (24.1%)	44 (75.9%)	6.8 (3.3)	6.7 (3.7)	2.2 (2.5)	9 (16.1%)	47 (83.9%)
Age	60–67 y	47	11 (23.4%)	36 (76.6%)	5.8 (3.9)	5.0 (4.1)	1.8 (2.3)	14 (31.1%)	31 (68.9%)
	68–75 y	51	9 (17.6%)	42 (82.4%)	4.3 (3.4)	5.9 (3.7)	1.8 (2.2)	22 (43.1%)	29 (56.9%)
BMI	≤ 30 kg/m^2	47	11 (23.4%)	36 (76.6%)	4.7 (4.0)	5.0 (3.9)	1.8 (2.0)	19 (41.3%)	27 (58.7%)
	> 30 kg/m^2	51	9 (17.6%)	42 (82.4%)	5.3 (3.5)	5.9 (3.8)	1.8 (2.5)	17 (34.0%)	33 (66.0%)

Data are presented as mean (SD) otherwise specified. CNV, conservative; TKR, total knee replacement; BMI, body mass index; DPA, Daily Physical activity; HADS, Hospital Anxiety and Depression Scale; KL, Kellgren–Lawrence; PCS, Pain Catastrophizing Scale; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index; y, years

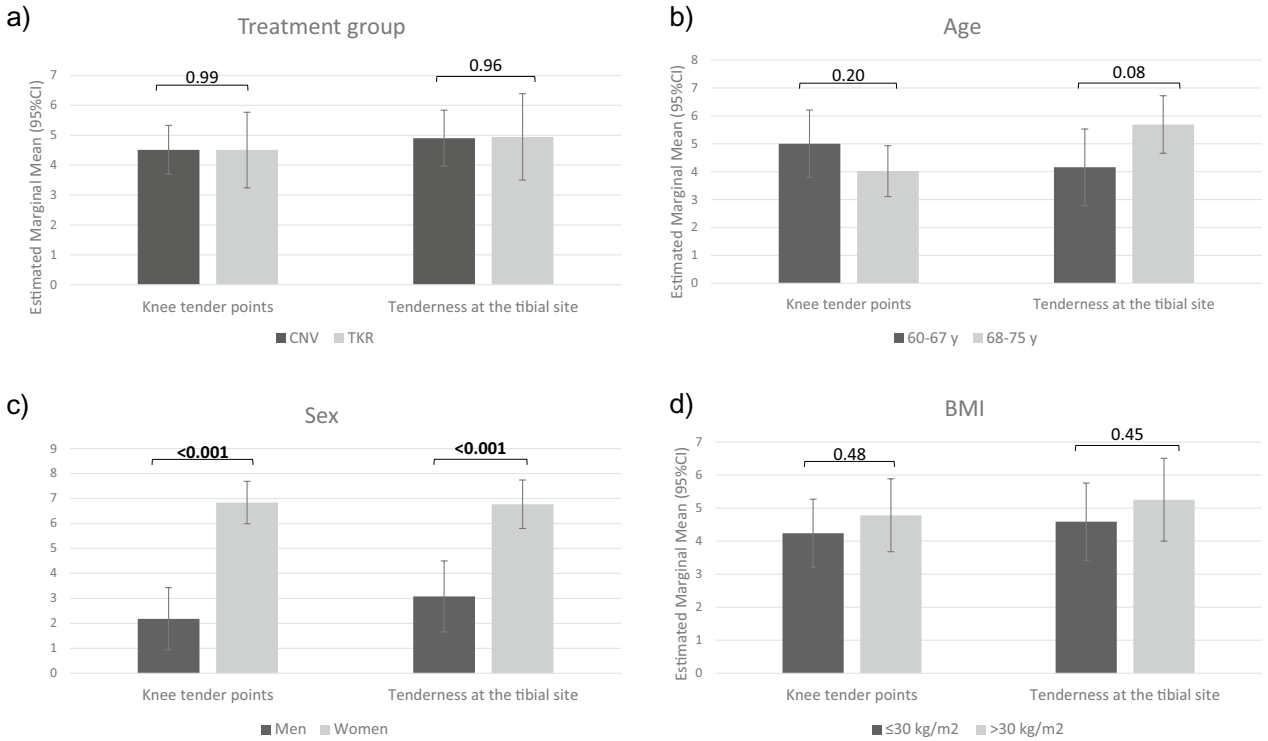

Fig. 2 Multivariate and univariate analyses of knee pain measures according to treatment group. Significant results are shown in bold. BMI, body mass index; CNV, conservative treatment approach; TKR, total knee replacement; y, years; kg, kilograms; m2, square meters

women 12.11, 95% CI 4.32–33.95; p value: 2.09*10^{-6}), but no differences were observed between CMG and TKR group (OR TKR 0.69, 95%CI 0.24–1.98; p value: 0.494) (Table 3).

Factors associated with TKR

We performed an analysis to calculate the association between TKR and the variables studied (Table 4). The WOMAC scale was significantly associated with TKR, with each one-point increase in the WOMAC score associated with a 5.4% higher odds of undergoing TKR (OR 1.054, 95% CI 1.022–1.085, p value = 6 × 10^{-6}). Also, the PCS scale showed a statistically significant association with a 7.3% higher odds of undergoing TKR (OR 1.073, 95% CI 1.022–1.126, p value = 0.004). Five points rise on the WOMAC and the PCS scale increased the risk of belonging to the TKR group by 29.83% and 42.24%, respectively. No other variables examined at either the

Table 3 Risk factors associated with clinical central sensitization: Multivariate logistic regression analysis

	OR (95% CI)	*p* value
Treatment	0.69 (0.24- 1.98)	0.494
Sex	12.11 (4.32- 33.95)	$2.09*10^{-6}$
Age	0.72 (0.26–1.97)	0.525
BMI	1.88 (0.69- 5.17)	0.219

Reference values for each factor are: treatment-CNV, sex-men, age-60–67 and BMI ≤ 30 kg/m^2. BMI, body mass index; CI, confidence interval; CNV, conservative treatment approach; OR, odds ratio

Table 4 Risk factors Associated with TKR

	OR (95% CI)	*p* value
WOMAC	1.054 (1.022–1.085)	$6{,}04 \times 10^{-6}$
HADS	1.014 (0.956–1.074)	0.647
PCS	1.073 (1.022–1.126)	0.004
DPA		
Household	0.985 (0.895–1.084)	0.762
Leisure	0.959 (0.874–1.052)	0.376
PPMs		
PPM1	0.893 (0.347–2.295)	0.814
PPM2	1.116 (0.427–2.917)	0.822
PPM3	2.921 (1.026–8.318)	0.045
PPM4	0.927 (0.365–2.350)	0.872
PPM5	2.547 (0.913–7.106)	0.074
PPM6	1.285 (0.502–3.290)	0.601
PPM7	0.809 (0.301–2.173)	0.675
PPM8	1.597 (0.621–4.110)	0.331
PPM9	0.668 (0.253–1.764)	0.416
PPM10	0.607 (0.211–1.751)	0.356
KTP	1.032 (0.896–1.190)	0.660
TTS	1.051 (0.932–1.186)	0.418
Temporal summation	1.000 (0.830–1.205)	0.999
Central sensitization	0.690 (0.242–1.969)	0.488

Adjusted Odds Ratios and 95% Confidence Intervals (adjusted for sex, age, and BMI). BMI, body mass index; DPA, daily physical activity; HADS, hospital anxiety and depression scale; KTP, knee tender points; PCS, pain catastrophizing scale; TTS, tenderness at the tibial site; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index

patient or knee level showed statistically significant differences in ORs between the two treatment groups.

Discussion

In this study comparing clinical traits between patients with knee osteoarthritis managed conservatively versus those undergoing TKR, we found significant differences in key clinical measures, with notable sex-specific variations in pain perception and treatment outcomes. Patients in the TKR group demonstrated consistently poorer outcomes, with notably higher scores in WOMAC, HADS, and PCS compared to those managed conservatively. Female patients exhibited heightened pain sensitivity and greater functional limitations compared to their male counterparts, suggesting potential differences in central pain processing mechanisms. This finding is particularly significant as these differences emerged despite both groups showing comparable radiographic severity of their condition and controlled by sex, BMI and age. Among all variables analyzed, the WOMAC score emerged with the strongest association with TKR, though its interpretation should consider sex-specific variations in symptom reporting and pain experience. These sex-based differences in clinical presentation and pain processing mechanisms suggest the need for personalized treatment approaches that account for sex-specific factors in pain sensitivity, functional limitations, and potential central sensitization when determining treatment pathways for knee osteoarthritis. The observed differences between sexes in both conservative management and surgical outcomes highlight the importance of considering sex-specific factors in clinical decision-making, potentially leading to more targeted and effective treatment strategies.

OA progression can be defined by different features [24], but it is nowadays mainly evaluated through the KL degree or joint space narrowing. Our findings suggest that radiological progression, although widely used as a marker for end-stage knee OA and TKR indication, may not be the most appropriate indicator for evaluating progression to surgical intervention [25]. Despite similar radiographic severity between groups, as evidenced by comparable KL grades, patients who underwent TKR demonstrated significantly higher WOMAC scores. This discordance between structural damage and clinical manifestations supports previous studies showing poor correlation between radiographic findings and symptom severity in KOA [26]. Our results indicate that clinical parameters, particularly WOMAC scores, may be more reliable predictors of progression to TKR than radiographic assessment alone. This finding has important implications for clinical practice, suggesting that treatment decisions should be based on a comprehensive evaluation of patient symptoms and functional limitations rather than solely on radiographic findings.

Our findings revealed significantly higher PCS scores in patients who underwent TKR compared to those managed conservatively. While the relationship between PCS and treatment selection has not been previously studied, extensive research has demonstrated that elevated PCS scores are associated with poorer post-TKR outcomes, including longer hospital stays, reduced quality of life, and increased risk of chronic pain [27–29]. Interventions

targeting pain catastrophizing, particularly cognitive behavioral therapy, have shown promising results in improving not only PCS scores but also knee function and pain management, with sustained long-term benefits [30–32]. A systematic review further supports this, indicating that perioperative interventions addressing psychological distress can positively impact post-TKR outcomes in terms of pain, function, and quality of life [33]. Given our observation of higher PCS scores in the TKR group, implementing pain coping strategies to address both WOMAC and PCS scores could potentially serve as an effective intervention to delay or prevent the need for TKR in certain patients, particularly those with elevated psychological distress.

Among the traditional risk factors associated with OA, our analysis revealed that sex was the only factor showing significant differences in clinical variables. Women exhibited higher WOMAC and PCS scores, indicating greater symptom severity and poorer quality of life compared to men. Additionally, women demonstrated significantly higher levels of pain sensitivity and were more likely to experience central sensitization. These findings suggest that biological and psychosocial factors contributing to pain perception and chronic pain syndromes may differ substantially by sex [34–37]. While these sex -based differences are well-documented in clinical settings, they are not observed in laboratory-induced pain studies with healthy subjects [38], Such differences have important implications for personalized treatment approaches in KOA management, suggesting a complex interplay of biological, psychological, and sociological factors in pain perception and experience [34, 39]. The sex -based differences in WOMAC scores are particularly relevant for clinical practice and research. WOMAC, which comprehensively assesses pain, stiffness, and function, is widely used to evaluate clinical progression and treatment response in OA. Current response criteria in OA clinical trials, whether using WOMAC or other scales (such as visual analog scale or Lequesne index) [40], typically define improvement thresholds as either a 20% reduction in scores [41, 42] or use other metrics like minimal perceptible clinical improvement [43, 44]. Our findings suggest that these response criteria should account for sex-based differences, as baseline WOMAC scores significantly differ between men and women. Interestingly, while we observed these sex-based differences in clinical measures, we found no interaction between gender and treatment choice. This indicates that gender differences did not influence the decision between conservative management and TKR in our study population since they both have higher levels in TKR group. However, different thresholds for males and females in WOMAC and PCS might be required to assess the need for TKR.

While age and BMI are traditionally considered significant risk factors for OA progression and TKR indication, our findings suggest that these factors did not significantly influence the clinical variables assessed in our study population. Neither age or BMI showed significant associations with WOMAC scores, pain measures, or psychological parameters between treatment groups. This observation aligns with recent research by Badley et al. [45], who found that age and obesity, unlike sex, did not correlate with an increased number of painful joint sites in OA patients.

These findings contrasts with traditional assumptions that advanced age and higher BMI [46] are among the primary contributors to both the progression of KOA and the likelihood of undergoing surgical intervention. In clinical practice, age is often considered a proxy for disease severity and cumulative joint degeneration, while BMI is strongly associated with mechanical stress on the joints and systemic inflammation. The lack of significant associations in this study may be explained by the relatively homogenous characteristics of our sample, as both treatment groups had comparable mean ages and BMI ranges. It is possible that age and BMI thresholds relevant to predicting TKR may not have been adequately captured within this range, or that other factors—such as pain perception, psychological distress, and central sensitization—play a more pivotal role in influencing treatment decisions in our cohort.

This discordance between established risk factors and clinical manifestations further emphasizes the complex, multifactorial nature of OA progression and highlights the importance of comprehensive patient assessment beyond traditional risk factors when considering treatment pathways. It suggests the need to reconsider their weight in clinical algorithms and guidelines, focusing instead on multidimensional assessments that incorporate both physical and psychosocial domains. The lack of significant associations between age, BMI, and treatment groups in our study contrasts with traditional assumptions about these factors being primary contributors to KOA progression and surgical intervention. While extensive literature supports age and obesity as key risk factors for KOA development and progression, our findings suggest their role in treatment decision-making may be less direct than previously thought. This unexpected finding might be explained by several factors: the relatively homogeneous characteristics of our sample population, the possibility that relevant age and BMI thresholds were not adequately captured within our study range, or that other factors—such as pain perception, psychological distress, and central sensitization—may play more pivotal roles in influencing treatment decisions in our cohort. Additionally, the presence of a significant three-way

interaction between sex, age, and BMI ($p=0.006$) suggests that these traditional risk factors may operate through more complex mechanisms than previously recognized, particularly when considering their combined effects on clinical manifestations and treatment outcomes.

In our analysis of interactions between demographic factors, we identified a significant three-way interaction between sex, age, and BMI ($p=0.006$). This interaction manifested primarily in WOMAC and PCS scores ($p=0.002$ for both). Notably, sex-based differences were most pronounced in patients presenting with a single risk factor (either advanced age or obesity), with women showing significantly higher WOMAC values than men in these subgroups. The presence of a single risk factor increased kinetic differences between the treatment groups, while the presence or absence of both made the difference disappear [18]. This complex interaction pattern suggests that the relationship between sex and clinical manifestations of KOA is modulated by the presence of other risk factors. Furthermore, women without risk factors (younger and non-obese) demonstrated significantly lower WOMAC and PCS values compared to women with one risk factor, highlighting the cumulative impact of these demographic characteristics on clinical outcomes.

Our analysis revealed that patients with higher WOMAC and PCS scores, particularly those reporting pain at the tibial site, had significantly higher odds of belonging to the TKR group, independent of sex, age, and BMI. These findings are particularly relevant given that knee arthroplasty demonstrates one of the highest rate variabilities among orthopedic procedures [47, 48]. This variability largely stems from the lack of standardized criteria regarding the functional status or disease burden that warrants surgical intervention. Additional factors contributing to this variability include regional differences in healthcare resources, physician preferences regarding clinical indications, and patient preferences [48, 49].

A multimodal approach combining physical therapies and psychological interventions may delay or even prevent the need for surgery. Conversely, patients with severe WOMAC scores and low PCS scores might benefit more directly from surgical evaluation. Ultimately, integrating WOMAC and PCS scores into clinical algorithms allows for a more comprehensive and personalized approach to KOA management, ensuring that treatment strategies address both the physical and psychological dimensions of the disease.

In the Spanish healthcare context, approximately 30% of TKR indications were found to be either incorrect or inadequately justified, with some regions showing up to 40% excess in TKR procedures compared to expected rates [49]. Notably, patients who underwent TKR in regions with lower surgery rates demonstrated higher average WOMAC scores compared to those in high-rate regions. This observation aligns with our findings and supports previous research suggesting that areas with higher TKR rates (and correspondingly lower WOMAC thresholds for surgery) likely include more cases of potentially inappropriate interventions [47]. While our study may not be entirely free from potential misclassification between conservative and surgical groups, our statistical analyses suggest overall appropriate patient stratification.

This study highlights several critical areas for future investigation to advance the management of KOA. First, prospective longitudinal studies are needed to validate the predictive utility of WOMAC and PCS scores in determining treatment pathways, including the decision to undergo TKR. Such studies could establish the temporal relationships between these scores, disease progression, and treatment outcomes, addressing the current limitations of cross-sectional designs. Second, future research should establish validated clinical thresholds integrating both WOMAC and PCS scores to guide treatment decisions: patients with lower WOMAC improvement scores and elevated PCS scores should first receive conservative management including psychological interventions, while those with higher domain-specific WOMAC thresholds and lower PCS scores may be prioritized for surgical evaluation, though these parameters require validation through prospective studies. Third, clinical trials exploring interventions targeting psychological factors, such as pain catastrophizing and central sensitization, could offer new therapeutic avenues. High PCS scores in particular have been linked to poorer outcomes, suggesting that addressing psychological distress through cognitive-behavioral therapy, mindfulness-based stress reduction, or similar interventions may improve patient-reported outcomes and delay the need for surgical interventions. Another promising area for future research involves exploring sex-specific treatment strategies. Given the observed differences in pain sensitivity and central sensitization between male and female patients, studies designed to tailor interventions based on sex may enhance the effectiveness of KOA treatments. Finally, multicenter studies with more heterogeneous samples are necessary to enhance the generalizability of findings and better capture the diversity of clinical presentations and treatment responses in KOA patients. These studies would allow for more robust conclusions and the development of widely applicable clinical algorithms.

This study has several strengths, including its comprehensive assessment of clinical variables, the use of validated measurement tools, and the careful matching of participants between groups for key demographic factors. The blinded evaluation of clinical measures helped minimize potential assessment bias.

Limitations

One limitation is the potentially limited generalizability of the findings due to the specific context of the study, including recruitment from a single center and the demographic characteristics of the sample. The study's findings may be limited in their generalizability to other populations or healthcare systems, as the data was collected from a single center in Barcelona, Spain, which may have specific demographic characteristics, clinical practices, and healthcare delivery patterns that differ from other regions or countries. Additionally, recruitment challenges, particularly within the male TKR subgroup, resulted in the exclusion of several potential participants due to prior meniscectomy. This selection bias may have systematically excluded patients with more severe disease progression or different clinical characteristics, potentially underestimating the true differences between treatment groups in male patients. The exclusion of patients with previous meniscectomy could have particularly affected our understanding of pain patterns and functional outcomes in men, as these procedures often indicate a history of more severe joint problems. This limitation may affect the generalizability of our findings and could have influenced the observed gender-specific differences in clinical outcomes and treatment responses.

Another important limitation is the inability to establish causality due to the cross-sectional design of the study. While we identified associations between higher WOMAC and PCS scores and TKR, the temporal sequence remains unclear—we cannot determine whether patients had elevated scores that led to choosing TKR, or if the impending surgery decision itself influenced their reported symptoms and psychological state. This temporal ambiguity limits our ability to use these scores as definitive predictive factors for surgical intervention.

Conclusions

The findings of this study provide valuable insights into the clinical characteristics and outcomes of patients undergoing CMG versus TKR for KOA. Clinical parameters, particularly WOMAC scores, are more strongly associated with TKR indication than traditional risk factors such as age and BMI. Patients undergoing TKR consistently showed higher WOMAC and PCS scores, despite similar radiographic severity, highlighting the importance of comprehensive clinical assessment in surgical decision-making. These results could inform the development of clinical guidelines by emphasizing the role of comprehensive patient evaluation, including functional impairment and pain perception, in decision-making for KOA management. Furthermore, the observed sex differences, particularly the increased risk of central sensitization and higher pain and functional impairment scores in women, highlight the need for sex-specific considerations in treatment planning and counseling. Integrating these findings into clinical algorithms could enhance personalized treatment strategies, ensuring that interventions are tailored to individual patient profiles. Additionally, the data could be utilized to refine shared decision-making tools, offering patients more precise information about the risks and benefits of surgical and non-surgical options, ultimately promoting informed choices in KOA management.

Abbreviations

ANOVA	Analysis of variance
BMI	Body mass index
CI	Confidence interval
CMG	Conservative Management Group
DPA	Daily physical activity
HADs	Hospital anxiety and depression scale
KL	Kellgren–Lawrence
KOA	Knee osteoarthritis
KTP	Knee tender points
MANOVA	Multivariate analysis of variance
OA	Osteoarthritis
OR	Odds ratio
PCS	Pain catastrophizing scale
PPT	Pressure pain threshold
SD	Standard deviation
TKR	Total knee replacement
TTS	Tenderness at tibial site
WOMAC	Western Ontario and McMaster Universities Osteoarthritis Index

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s13018-025-05552-2.

Supplementary file 1.

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Authors contributions

FO conceptualized, designed methodology, performed formal analysis, conducted investigation, curated data, wrote original draft, and administered the project. Additionally, contributed to patient recruitment and performed clinical assessments. LT conducted statistical analysis, interpreted data,

contributed to methodology development, and critically revised the manuscript for important intellectual content. JM supervised the project, provided clinical expertise, validated methodology, and contributed to manuscript revision and final approval. All authors reviewed and approved the final version of the manuscript and agree to be accountable for all aspects of the work.

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Availability of data and materials
The datasets generated and analyzed during the current study are not publicly available due to privacy and ethical restrictions but are available from the corresponding author upon reasonable request with appropriate institutional review board approval and data sharing agreement.

Declarations

Ethics approval and consent to participate
The study was conducted in accordance with the principles of the Declaration of Helsinki. The protocol followed Good Clinical Practice guidelines and was approved by the Ethical Committee of Clinical Research of the Parc de Salut Mar of Barcelona (reference number: 2016/6747/I). All participants provided written informed consent prior to their inclusion in the study.

Consent for publication
All participants provided written informed consent for their data to be used in this research and subsequent publication. All data have been presented in aggregate form and no individually identifiable data is reported in this publication.

Competing interests
The authors declare that they have no competing interests.

Author details
[1]Rheumatology Service, Hospital del Mar, Passeig Marítim, 08003 Barcelona, Spain. [2]Hospital del Mar Research Institute, Barcelona, Spain. [3]Centro Médico Teknon, Barcelona, Spain. [4]BCN MedTech, DTIC, Universitat Pompeu Fabra, Barcelona, Spain.

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